REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative, as noted below.

Status of the Claims

Pending claims

Claims 1, 2, 4 to 9, and 14 to 55 are pending.

Claims canceled and added in the instant amendment

Claims 17, 21 and 33 are canceled without prejudice or disclaimer; and new claims 56 to 59 are added. Thus, after entry of the instant amendment claims 1, 2, 4 to 9, 14 to 16, 18 to 20, 22 to 32 and 34 to 59 will be pending and under consideration.

Outstanding Rejections

Claims 8 and 53 (and their dependent claims 9 and 14) are rejected under 35 U.S.C. §101 as alleged being drawn to non-statutory subject matter. Claims 1, 2, 5, 17, 19 to 23, 27 to 37, 40 and 54 (and their dependent claims) are rejected under 35 U.S.C. §112, second paragraph. Claims 1, 2, 4 to 9, and 14 to 55 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement of section 112, first paragraph (see pages 6 to 12 of the OA). Claims 27 to 30 (see pages 12 to 16 of the OA) and 40 to 43 (see pages 16 to 17 of the OA) are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement of section 112, first paragraph. Claims 1, 2, 4 to 9 and 14 to 55 are rejected under 35 U.S.C. §102(e), as allegedly anticipated by US patent 6368844; US pub 2003/0155550; or, US pub 2003/0078397. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the claim amendments

The specification sets forth an extensive description of the invention in the new and amended claims. For example, support for claims drawn to probes capable of identifying or

isolating nucleic acids encoding a polypeptide having endoglucanase or cellulase activity can be found, inter alia, on page 8, lines 9 to 28; page 9, lines 19 to 23; the paragraph spanning pages 13 to 14; page 20, lines 15 to 17, of WO 97/44361 (the publication of PCT/US97/08793). Accordingly, no new matter has been added by way of these amendments.

Claim objections

Claims 19, 27 to 28, 40 and 54 are objected to for reasons set forth on page 3, of the OA. The instant amendment addresses this issue.

Issues under 35 U.S.C. §101 – statutory subject matter

Claims 8 and 53 (and their dependent claims) are rejected under 35 U.S.C. §101 as alleged being drawn to non-statutory subject matter, for reasons set forth on page 4 of the OA. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, second paragraph

Claims 1, 2, 5, 17, 19 to 23, 27 to 37, 40 and 54 (and their dependent claims) are rejected under 35 U.S.C. §112, second paragraph, for reasons set forth in the OA on page 4, last two lines, to page 6, line 2, of the OA. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph, enablement requirement

The rejection of claims 1, 2, 4 to 9, and 14 to 55 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement of section 112, first paragraph, has been maintained (see pages 6 to 12 of the OA; pages 3 to 9, of the office action of April 19, 2005; pages 6 to 9 of the office action of July 22, 2004).

The Office did state that the specification does enable an endoglucanase having the amino acid sequence of SEQ ID NO:46, encoded, e.g., by the nucleic acid sequence SEQ ID NO:45, and vectors and host cells comprising this polynucleotide.

However, the Office alleged that the specification does not reasonably enable any of the several claimed genera of polypeptides or polynucleotides having 97%, 95%, 90% or 70% sequence identity to an exemplary sequence of the invention (SEQ ID NO:45/46), or the claimed subsequences thereof (see page 6 of the OA).

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, any of the several claimed genus of polypeptides or polynucleotides having 97%, 95%, 90% or 70% sequence identity to SEQ ID NO:45/46 – and in support have provided argument, evidence and expert declaration in previous responses, all of which are expressly incorporated herein (see, e.g., pages 10 to 16, of their October 13, 2005, response). Applicants also respectfully averred that the Patent Office did not met its initial burden to establish a reasonable basis to question the enablement provided for the claimed invention, and specifically addressed how the art used to support the Office's enablement rejection was not sufficient to rebut the presumptively enabled specification.

However, only to expedite prosecution of this application, Applicants further limit the scope of the genus of template polypeptides used to practice the claimed invention to a genus having at least 90% sequence identity to SEQ ID NOs: 45/46.

Because Applicants' previous responses are expressly incorporated herein, they will not be reiterated in this submission. However, because one of the Office's concerns is that it would have taken undue experimentation to make any of the claimed genus of nucleic acids or polypeptides of this invention, Applicants believe a brief review of (at least some of) their arguments, and some additional argument, in light of the factors to be used for determining undue experimentation as set forth in In re Wands would be helpful:

The breadth of the claims

The Office maintains that specification did not enable claims comprising any of the several claimed genus of polypeptides or polynucleotides having 97%, 95%, 90% or 70% sequence identity to SEQ ID NO:45/46.

While Applicants respectfully traverse, only to expedite prosecution of this application, Applicants further limit the scope of the genera of nucleic acids and polypeptides used to practice this invention to a genera having at least 90% sequence identity to SEQ ID NO:1, or subsequences thereof.

The amount of direction or guidance presented and the existence of working examples

The Office maintained that the specification did not sufficiently enable the skilled artisan to practice the claimed invention because, inter alia, the specification did not provide specific

knowledge or guidance as to which protein or nucleic acid structure (sequence) could be modified to produce the claimed genus of enzymes or the nucleic acids that encode them, and without such guidance it would have required undue experimentation to practice the invention (see, e.g., page 11, lines 6 to 11, and 15 to 18, of the OA).

Applicants respectfully maintained (see previous responses) that it was not necessary to provide specific knowledge or guidance as to which protein or nucleic acid structure (sequence) could be modified to make or use the claimed genus of enzymes or the nucleic acids that encode them. For example, in their last response Applicants demonstrated that routine, simple sequence alignment comparison of known endoglucanase and cellulase sequences would have identified regions of identity and dissimilarity to provide guidance to the skilled artisan as to which sequences could be changed, or not changed, to generate structural and/or functional variations of an exemplary endonucleases of the invention, and provided an example of such a sequence alignment. Further guidance regarding endoglucanase structure and active sites was available to the skilled artisan at the time of the invention in the form of three dimensional crystal structures, and Applicants listed a few examples. Thus, if the skilled artisan desired some guidance as to which amino acid residues could be modified to obtain structural or functional variants of an enzyme of the invention, that information was readily available at the time of the invention.

The state of the art, relative skill in the art, and predictability of the art

The Office also maintained its allegation that, inter alia, it was not routine in the art to screen for multiple substitutions or multiple modifications (see page 8, lines 16 to 22, for full text). Applicants traversed and submitted an expert declaration by Dr. Short. Dr. Short declared, inter alia, that it that the state of the art at the time of the invention and the level of skill in the art for screening enzymes for endoglucanase/ cellulase activity was very high; procedures for making endoglucanase and cellulase enzyme fragments and sequence variations, e.g., with substitutions, deletions, insertions, and additions, were routine in the art at the time of the invention; assays for identifying endoglucanase and cellulase enzyme fragments were conventional and routine in the art at the time of the invention; assays for identifying variant polypeptides having endoglucanase and cellulase activity were conventional and routine in the art at the time of the invention; and, use of

high through-put screening assays is an example of the high state of art at the time of the invention for screening polypeptides for endoglucanase and cellulase enzyme activity.

Applicants also noted that assays for identifying polypeptides having endoglucanase activity are described in the specification, e.g., on page 17, line 6 to page 18, line 7. Dye-based techniques can be used in cup-plate diffusion assays with excellent sensitivity for the determination of endoglucanase activity in culture filtrates or during enzyme purification steps (see first paragraph, page 18), as further noted in Example 1, page 36. Dr. Short declared that endoglucanase activity assays also were well known in the art at the time of the invention, e.g., as described in USPNs 4,081,328; 4,904,599; 5,110,735; 5,366,884.

The quantity of experimentation needed to practice the invention

Applicants have maintained that the specification provided reasonable enablement regarding the structure and sequence of the genus of nucleic acids used to practice the claimed methods. Whether large numbers of compositions (e.g., a genus of template nucleic acids) must be screened to determine if one can be used to practice the claimed invention is irrelevant to an enablement inquiry. As discussed in Applicants' previous responses, enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue". Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). The proper legal test is that the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). See MPEP §2164.08, pg 2100-205, 206, 8th ed., rev. 3, Aug. 2005. `The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' " In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)). MPEP §2164.06(b), pg 2100-203, 8th ed., rev. 3, Aug. 2005.

The facts in In re Wands are sufficiently analogous to the instant application to help illustrate this point, as explained in the MPEP (§2164.06(b), pg 2100-203, 8th ed., rev. 3, Aug. 2005):

> (B) In In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the court reversed the rejection for lack of enablement under 35 U.S.C. 112, first paragraph, concluding that undue experimentation would not be required to practice the invention. The nature of monoclonal antibody technology is such that experiments first involve the entire attempt to make monoclonal hybridomas to determine which ones secrete antibody with the desired characteristics. The court found that the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the application was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HBsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims.

In In re Wands, after considering all the factors related to the enablement issue, the court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." Id., 8 USPQ2d at 1407. In In re Wands, it was not necessary to provide a method to routinely identify *every* monoclonal antibody hybridoma made in any particular production round, or *every possible* monoclonal antibody that could bind the exemplary antigen. Nor was it necessary to produce a working specie after very antibody-making procedure. In fact, in In re Wands, the screening protocol was found sufficiently enabling even though only one antibody was identified after running three procedures.

Analogous to In re Wands, it is not necessary that the specification or the state of the art at the time of the invention describe a protocol where every, or even most, attempts at making a template nucleic acid (within the limitations of the claimed invention) are successful. Because proper legal test is that the scope of enablement must only bear a "reasonable correlation" to the scope of the claims, as in In re Wands, methods for making the genus of template nucleic acids used in the claim methods are sufficiently enabling if a reasonable number of claimed species are successfully made by protocols known in the art and/or described in the specification. Protocols for endoglucanase activity screening were well known in the art at the time of the invention, and assays

for identifying polypeptides having endoglucanase activity are described in the specification, e.g., on page 17, line 6 to page 18, line 7; first paragraph, page 18; Example 1, page 36, of the specification.

Thus, using the teaching of the specification and other protocols known in the art at the time of the invention one skilled in the art could have successfully practiced the invention without undue experimentation, including making and using the claimed genus of endoglucanase-encoding nucleic acids without undue experimentation. In other words, methods for making and screening for endoglucanases were sufficiently sophisticated and well known at the time of the invention that one of skill in the art could have made the genus of template nucleic acids used in the claim methods without "undue experimentation", according to the appropriate legal definition of this term, e.g., as in In re Wands.

Furthermore, also analogous to In re Wands, because the specification provided direction and guidance on how to practice the claimed invention and all of the methods needed to practice the invention were well known, and there was a high level of skill in the art at the time the application was filed, the instant specification did provide reasonable enablement commensurate with the scope of the claimed invention. Accordingly, the enablement rejection under section 112, first paragraph, can be properly withdrawn.

Issues under 35 U.S.C. §112, first paragraph, written description requirement

The rejection of claims 27 to 30 (see page 12, line 9, to page 16, line 15, of the OA), and claims 40 to 43 (see page 16, line 16, to page 17, line 21) under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement of section 112, first paragraph, is maintained.

Applicants respectfully maintain that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing, and in previous responses, all of which are expressly incorporated herein (see, e.g., pages 16 to 19, of their October 13, 2005, response) have provided argument in support.

The Office remains concerned that the claimed invention encompasses a "large variable genus" (see, e.g., page 12, line 17, of the OA). The instant amendment addresses this issue by narrowing the scope of the claimed genera of polypeptides; for example, amended claims 27 is directed to a genus of polypeptides having endoglucanase or cellulase activity comprising at least 30 amino acid residues of a polypeptide having at least 90% sequence identity SEQ ID NO:46. Claim 28 as amended is directed to a genus of polypeptides having comprising at least 50 amino acid residues of a polypeptide having at least 90% sequence identity to SEQ ID NO:46.

Applicants also wish to clarify additional issues that remain a concern to the Office. Regarding claims 27 to 30, on page 14, lines 8 to 11, of the OA, the Office implies that claimed fragments of claims 27 to 30 may encompass non-active polypeptides. In fact, the claims are expressly limited only to polypeptides having endoglucanase or cellulase activity.

Also regarding claims 27 to 30, on page 15, lines 13 to 14, of the OA, the Office implies that the claimed genera of polypeptides are "short on structure and recite only function." In fact, the claims expressly set forth the structural parameters of all, or the active portion, of the claimed polypeptides – for example, in one aspect of claims 27 or 28, the invention encompasses a genus of polypeptides having endoglucanase or cellulase activity consisting of 30 or 50 amino acid residues of a polypeptide having 90% sequence identity SEQ ID NO:46.

This may also clarify the Office's comment on page 14, lines 13 to 14, where it is implied that the entire structure of the claimed polypeptide is not described in the claim. In fact, the entire structure of the polypeptide having endoglucanase or cellulase activity, or at least the active portion thereof, is expressly set forth in the claims, notwithstanding the fact that that the term "comprising" is used. The claims are clear that it is the described and claimed sequence that has the enzymatic activity. New claims 57 and 59 emphasize this point. As noted in their previous response, Applicants respectfully aver that it is not the law that unrecited subject matter in a claim using the opened-ended term "comprising" be described to satisfy the written description rejection of section 112, first paragraph.

Regarding claims 40 to 43, as amended they encompass a genus of probes for identifying or isolating a nucleic acid encoding a polypeptide having endoglucanase or cellulase activity, the probe(s) comprising at least 15 contiguous nucleotides of a sequence encoding a polypeptide having

endoglucanase or cellulase activity and having at least 90% sequence identity to SEQ ID NO:45, wherein the probe(s) hybridize under stringent conditions to the polynucleotide sequence SEQ ID NO:45. On page 17, line 1, of the OA, the Office implies that the specification does not contain any disclosure of the function of all DNA sequences encompassed by the claim. In fact, the claim expressly only includes probes for identifying or isolating a nucleic acid encoding a polypeptide having endoglucanase or cellulase activity. While Applicants acknowledge that all species members of a genus of biological sequences must have a structure-function relationship, they respectfully aver that the linking functional limitation of the members of the genus does not necessary have to be its natural biological function, but can be another function, e.g., as a research tool, for example, a probe to isolate or identify a protein-encoding sequence.

Finally, on page 17, lines 17 to 21 of the OA, the Office notes that because the claims 40 to 43 use the term "comprising", a composition encompassing the claimed probes might include additional sequences that do not hybridize under stringent conditions to the polynucleotide sequence SEQ ID NO:45. Applicants confirm that indeed this is true, noting that because the term "comprising" was used other materials and compositions may also be attached to the claimed probes (for example, a fluorescent molecule or tag). However, Applicants respectfully aver that it is not the law that unrecited subject matter in a claim using the opened-ended term "comprising" be described to satisfy the written description rejection of section 112, first paragraph. Such a requirement would necessarily always obviate use of the term "comprising".

Accordingly, Applicants respectfully submit that the pending claims as amended meet the written description requirement under 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102(e)

Claims 1, 2, 4 to 9 and 14 to 55 are rejected under 35 U.S.C. §102(e), as allegedly anticipated by US patent 6,368,844; US pub 2002/0155550; or, US pub 2003/0078397 (the OA included a typo: 2002/0078397).

The instant application claims priority under 35 U.S.C. §371 to Patent Convention Treaty (PCT) International Application Serial No: PCT/US97/08793, filed May 22, 1997, which claims benefit of priority to U.S. Patent Application Serial No. ("USSN") 08/651,572, filed May 22, 1996, now U.S. Patent No. 5,789,228, issued August 4, 1998. In the instant application, SEQ ID NO:45

can claim priority to Patent Convention Treaty (PCT) International Application Serial No: PCT/US97/08793, filed May 22, 1997. However, as explained in detail, below, because none of the cited documents US patent 6,368,844; US pub 2003/0155550; or, US pub 2003/0078397, disclose SEQ ID NO:45/46 before May 22, 1997, none of these cited documents are prior art the instant application:

- US patent 6,368,844, filed Aug 13, 1998:

This application is a continuation of USSN 08/949,026, filed Oct. 10, 1997, which claims priority to U.S. provisional app. no. 60/056,916, filed Dec. 6, 1996. However, USSN 60/056,916 does not disclose SEQ ID NO:45; and the earliest disclosure of (priority for) SEQ ID NO:45 (which is the equivalent of SEQ ID NO:60 in the US patent 6,368,844 family) is the filing date of USSN 08/949,026, on October 10, 1997.

- US pub 2002/0155550; filed: Apr 9, 2002

This application claims priority to several applications, including USSN 08/949,026 and its earliest priority document U.S. provisional app. no. 60/056,916, filed December 6, 1996. However, USSN 60/056,916, filed **Dec 6, 1996, does NOT contain** SEQ ID NO:45; and the earliest disclosure of (priority for) SEQ ID NO:45 (which is the equivalent of SEQ ID NO:60 in the US pub 2002/0155550 family) is the filing date of USSN 08/949,026, on October 10, 1997.

- US pub 2003/0078397; filed: Mar 6, 2002.

This application is a continuation of USSN 09/910,579 filed July 20, 2001, which is a continuation-in-part of USSN 09/134,078, filed August 13, 1998, which is a continuation of USSN 08/949,026, filed October 10, 1997, claims priority under 35 USC §119(e)(1) to U.S. provisional app. no. 60/056,916, filed December 6, 1996. However, USSN 60/056,916, filed **Dec 6, 1996, does NOT contain** SEQ ID NO:45; and the earliest disclosure of (priority for) SEQ ID NO:45 (which is the equivalent of SEQ ID NO:60 in the US pub 2003/0078397 family) is the filing date of USSN 08/949,026, filed on October 10, 1997.

Thus, because none of the cited documents US patent 6,368,844; US pub 2003/0155550; or, US pub 2003/0078397, disclose SEQ ID NO:45/46 before December 6, 1996, these documents are not prior art the instant application, and the rejection under section 102 can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §101; 35 U.S.C. §112, first and second paragraphs; and, 35 U.S.C. §102. In view of the above, claims in this application after entry of the instant amendment are believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 564462000502. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 7205133.

Dated: June 26, 2006

Respectfully submitted,

By _____

Gregory P. Einhorn
Registration No.: 38,440
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego CA 92130-2040
(858) 720-5133 direct line
general office 858 720 5100
fax direct 858 523 5933
fax office 858 720 5125
(858) 720-5133
email geinhorn@mofo.com